Complete Summary

GUIDELINE TITLE

(1) Neoplastic complications of HIV infection. (2) July 2007 addendum.

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Neoplastic complications of HIV infection. New York (NY): New York State Department of Health; 2007 Jul. 19 p. [39 references]

New York State Department of Health. Neoplastic complications of HIV infection. New York (NY): New York State Department of Health; 2007. 33 p. [94 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Neoplastic complications of human immunodeficiency virus (HIV) infection including:

- Acquired immunodeficiency syndrome (AIDS)-associated lymphomas
- Kaposi's sarcoma
- Cervical dysplasia and cancer
- Anal dysplasia and cancer
- Non-AIDS-defining cancers

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Screening
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Oncology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To help primary care clinicians caring for human immunodeficiency virus (HIV)-infected patients to understand the presentation, evaluation, and therapeutic options available for patients with common HIV-associated and non-HIV-related malignancies

TARGET POPULATION

Human immunodeficiency virus (HIV)-infected patients with neoplastic complications

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Screening

1. Routine blood work including complete blood count, serum liver enzymes, serum creatinine, calcium, phosphorus, uric acid
2. Contrast-enhanced magnetic resonance imaging (MRI)
3. Lumbar puncture with cerebrospinal fluid analysis
4. X-rays, scan, and/or bronchoscopy
5. Biopsy of lymph nodes or lesions
6. Annual skin and oral cavity examination
7. Endoscopic evaluation if indicated
8. Screening for cervical dysplasia (Pap tests)
9. Referral to colposcopy and further evaluation if Pap test result is abnormal
10. Screening for anal cancer (visual inspection, digital rectal examination, anal cytology)

11. High-resolution anoscopy
12. Risk-reduction behaviors and age-appropriate screening recommendations, such as mammography and colonoscopy

Management/Treatment

1. Management of lymphomas
    - Concurrent highly active antiretroviral therapy (HAART) and chemotherapy for lymphoma
    - Referral to research centers for protocol participation
    - Considering experimental high-dose therapy and stem cell transplantation for patients with relapsed or refractory disease with good performance status and well-controlled human immunodeficiency virus (HIV) disease
    - Palliative radiation and dexamethasone in B-cell central nervous system lymphoma
    - Adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) therapy for Hodgkin's disease
2. Management of Kaposi's sarcoma
    - Optimization of HIV control
    - Chemotherapy consisting of either liposomal anthracycline or paclitaxel
    - Local topical injectable, or radiation therapy of cutaneous lesions
    - Low-dose interferon alpha
    - Participation in clinical trials of novel therapeutic agents
3. Management of cervical cancer
    - Referral of HIV-infected women to gynecologic oncologist or surgeon for appropriate staging and treatment
4. Management of anal cancer
    - Referral to oncologist
    - Combined modality therapy with concurrent radiation and combination chemotherapy
5. Management of non-acquired immunodeficiency syndrome (AIDS)-defining cancers
    - Individualized treatment as in patients without HIV infection

MAJOR OUTCOMES CONSIDERED

- Effectiveness of treatment in terms of response rate, disease-free and overall survival rate, and relapse rates
- Sensitivity, specificity and positive and negative predictive values of diagnostic tests

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence for Recommendation

I. Evidence from one or more properly randomized, controlled trial
II. Evidence from one or more well-designed clinical trial without randomization; from cohort or case-controlled studies
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with HIV infection. Committees* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees* rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

* Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection
- Dental Standards of Care Committee
- Mental Health Committee
- Women's Health Committee
- Substance Use Committee
- Physician's Prevention Advisory Committee
- Pharmacy Committee

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Acquired Immunodeficiency Syndrome (AIDS)-Associated Lymphomas

Diagnosis

Clinicians should perform imaging studies to evaluate for nonpalpable, pathologic adenopathy when patients present with unexplained constitutional symptoms that last for more than 2 weeks, such as weight loss, fevers, and night sweats. (**I**)

Clinicians should obtain biopsies of lymph nodes that are newly developed, pathologically enlarged (typically >2 cm), or progressively enlarging. (**I**)

Clinicians should have diagnoses confirmed by experts at a referral center or commercial laboratory whenever possible. (**III**)

Concurrent Highly Active Antiretroviral Therapy (HAART) and Lymphoma Therapy

Patients currently receiving HAART should continue their antiretroviral (ARV) regimen while undergoing therapy unless there are other indications for an

interruption of ARV treatment. (**III**) If ARV therapy is interrupted in patients receiving ARV medications with prolonged half-lives, such as non-nucleoside reverse transcriptase inhibitors (NNRTIs), clinicians should consult with an human immunodeficiency virus (HIV) Specialist for guidance on how to avoid the emergence of resistance.

If possible, clinicians should avoid using zidovudine in patients receiving chemotherapy. (**III**)

Clinicians should individualize prophylaxis for opportunistic infections in patients receiving chemotherapy. (**I**) When patients present with CD4 counts in the normal range (400-1400 cells/mm^3), prophylaxis should be dictated by the severity of immunosuppression anticipated from the chemotherapy regimen.

Key Point:

Although chemotherapeutic drugs may have overlapping toxicities with ARV drugs, it is common practice to continue HAART during chemotherapy. However, because experience with newer ARV medications and cancer chemotherapy is limited, the clinicians should maintain vigilance for unusual or unusually severe toxicities.

Specific Lymphoma Histologies

B-Cell Diffuse Large Cell Lymphoma (B-DLCL)

Treatment

Whenever possible, HIV-infected patients should be treated with the same full-dose chemotherapy regimens that would be used in the absence of HIV infection. (**III**)

Clinicians should refer patients to research centers for protocol participation whenever feasible. (**III**)

Relapsed and Primary Refractory Disease

Clinicians should consider experimental high-dose therapy and stem cell support for patients with relapsed or refractory disease who have good performance status and well-controlled HIV disease. (**III**) Treatment for other patients remains palliative.

Primary Effusion Lymphoma

Key Point:

Specific recommendations for treatment cannot be made on the basis of clinical trial, although therapy directed at B-DLCL is reasonable.

Primary B-Cell CNS Lymphoma

Treatment for primary B-cell central nervous system (CNS) lymphoma is primarily palliative radiation and dexamethasone, (**III**) although a small, highly selected group of patients may benefit from chemotherapy.

Burkitt's and Burkitt's-like Lymphoma

There is no uniformly accepted treatment for this highly aggressive form of lymphoma. Clinicians should consider the use of regimens applicable to the non-HIV-infected population, particularly if the CD4 count is high and the associated HIV comorbidities are few. (**III**)

Plasmablastic Lymphoma

There are no known successful treatments for plasmablastic lymphoma.

Hodgkin's Disease

Both ABVD chemotherapy (adriamycin, bleomycin, vinblastine, dacarbazine) and the more recently described Stanford V regimen are reasonable treatments for HIV-associated Hodgkin's disease. (**I**)

Clinicians should consider patients with relapsed or primary refractory Hodgkin's disease and well-controlled HIV for research protocols of intensive therapy with peripheral blood stem cell support. (**III**)

Indolent Lymphoma

Treatment should be commensurate with the lymphoma diagnosis (**I**) unless precluded by HIV comorbidities (**III**).

(See Appendix A in the original guideline document for treatment options for HIV-associated lymphomas.)

Kaposi's Sarcoma (KS)

Diagnosis

When the clinician suspects KS based on visual inspection, biopsy of at least one lesion should be obtained to confirm the diagnosis and to differentiate KS from other pigmented lesions. (**III**)

Cutaneous KS

As part of the annual skin examination, the clinician should examine the oral cavity and the entire skin surface, including the soles of the feet, scalp, external genitalia, and ears, for the presence of abnormal pigmented lesions. (**I**)

Nodal KS

Key Point:

Unless lymph nodes are sufficiently enlarged or asymmetric to warrant biopsy for exclusion of lymphoma, there is no need to routinely biopsy enlarged lymph nodes in patients with biopsy-proven KS elsewhere.

Gastrointestinal KS

In the absence of gastrointestinal symptoms, radiographic or endoscopic evaluation of the gastrointestinal tract is not recommended for routine staging of KS (**III**). However, when a patient with known cutaneous KS presents with unexplained gastrointestinal symptoms (particularly pain, bleeding, or signs of obstruction), the clinician should perform an endoscopic evaluation of the upper and/or lower gastrointestinal tract (**I**).

Pulmonary KS

When a patient with known cutaneous KS presents with dyspnea, wheezing, and/or hemoptysis, clinicians should perform a differential diagnosis for pulmonary KS by obtaining x-rays, scans, and/or bronchoscopy to exclude infections and other neoplastic processes (e.g., lymphoma, lung cancer). (**I**)

Treatment

Unless immediate chemotherapy is indicated, the clinician should first attempt to optimize HIV control in patients receiving no or suboptimal ARV therapy because KS may respond to this alone (**I**). Patients should also receive prophylaxis for and treatment of opportunistic infections (**I**) (for more information on infectious diseases associated with HIV infection, see the National Guideline Clearinghouse [NGC] summaries of the New York State Department of Health [NYSDOH] guidelines Mycobacterial infections and Infectious complications associated with HIV infection: parasitic infection).

Clinicians should use chemotherapy consisting of either a liposomal anthracycline (liposomal doxorubicin or liposomal daunorubicin) or paclitaxel as first-line therapy for patients with the following KS manifestations (**I**):

- Documented pulmonary KS
- Symptomatic visceral KS
- Extensive, symptomatic KS-associated lymphedema
- Extensive and symptomatic or rapidly progressive cutaneous KS

For patients who do not require immediate chemotherapy for life-threatening or highly symptomatic KS, clinicians should use one of the following approaches (**I**):

- Local topical, injectable, or radiation therapy of cutaneous lesions
- Low-dose interferon alfa
- Participation in clinical trials of novel therapeutic agents targeting the pathogenic mechanisms involved in KS

Key Point:

Advanced HIV infection itself is not a contraindication to chemotherapy for treatment of KS.

(See Appendix A in the original guideline document for treatment options for HIV-associated KS.)

Cervical Dysplasia and Cancer

Cervical Dysplasia

Screening for Cervical Dysplasia

Clinicians should perform a gynecologic examination in HIV-infected women during the baseline evaluation. Pap tests should be performed, regardless of the woman's sexual orientation. It should be performed during the initial physical examination, repeated at 6 months, and then repeated annually, as long as the results are normal (see Table 2 in the original guideline document).

Women with abnormal Pap tests should be referred for colposcopy and further evaluation that may include human papilloma virus deoxyribonucleic acid (HPV DNA) testing, cervical biopsy, cervical curettage, and endometrial biopsy, depending on cell type and the degree of the cytological abnormality.

Cervical Cancer

Management of Cervical cancer

Clinicians should refer HIV-infected women to a gynecologic oncologist or surgeon trained in management of cervical cancer when possible. Appropriate staging, management, and therapy for cervical cancer should be determined by a gynecologic oncologist or clinician with similar training and experience.

(See Appendix A in the original guideline document for treatment options for HIV-associated cervical cancer.)

Anal Dysplasia and Cancer

Screening and Diagnosis

At baseline and as part of the annual physical examination for all HIV-infected adults, regardless of age, clinicians should:

- Inquire about anal symptoms, such as itching, bleeding, diarrhea, or pain
- Perform a visual inspection of the perianal region
- Perform a digital rectal examination (**III**)

Clinicians should refer women with cervical high-grade squamous intraepithelial lesion (HSIL) and any patient with abnormal anal physical findings, such as warts, hypopigmented or hyperpigmented plaques/lesions, lesions that bleed, or any other lesions of uncertain etiology, for high-resolution anoscopy and/or examination with biopsy of abnormal tissue.

Clinicians should obtain anal cytology at baseline and annually in the following HIV-infected populations (Frisch et al., 2001; Frisch, Biggar, & Goedert, 2000; Anderson et al., 2005; Goncalves et al., 2005; Caselli et al., 2005; Gaggin, Lauchin, & Steben, 2005; Diaz-Arrastia & Harrington, 2005; Head, 2005; Berry, 2005; Konstantinopoulos, Schlecht, & Bryan, 2006; Peters, Mack, & Bernstein, 1984; Melbye & Sprogel, 1991; Frisch, Olsen, & Melbye, 1994; Rabkin et al., 1992; Abramovitz et al., 2007):

- Men who have sex with men
- Any patient with a history of anogenital condylomas
- Women with abnormal cervical and/or vulvar histology

Key Point:

If the digital rectal examination is performed in conjunction with anal cytology and/or high-resolution anoscopy (HRA), the cytology must be obtained first, *before* lubrication is introduced into the anal canal.

Anal Cytology Screening

Clinicians should refer patients with abnormal anal cytology for high-resolution anoscopy and possible biopsy.

Treatment of Anal High-Grade Squamous Intraepithelial Lesions

Patients should receive post-treatment serial monitoring with annual HRA.

Treatment of Anal Cancer

Primary care clinicians should refer HIV-infected patients with anal cancer to an oncologist for treatment.

For patients with untreated invasive anal cancer without evidence of distant metastases and CD4 counts >200 cells/mm^3, combined modality therapy with concurrent radiation and combination chemotherapy should generally be administered. *In situ* carcinoma is not treated with radiotherapy or chemotherapy.

(See Appendix A in the original guideline document for treatment options for HIV-associated anal cancer.)

Non-AIDS-Defining Cancers

Clinicians should promote risk-reduction behaviors, such as smoking cessation, and should adhere to standard, age-appropriate screening recommendations, such as mammography and colonoscopy, that apply to the non-HIV-infected population. (**I**)

Although there are no specific guidelines for the treatment of incident, non-AIDS-defining cancers in HIV-infected patients and treatment needs to be individualized, clinicians should not a priori treat such patients with less

aggressive therapy than would be used in similarly staged patients without HIV infection. (**III**)

Key Point:

Clinicians should be vigilant for the development of cancers that are not specifically associated with HIV infection but that are common in the general population, such as lung cancer, breast cancer, colorectal cancer, prostate cancer.

Definitions:

Quality of Evidence for Recommendation

I. Evidence from one or more properly randomized, controlled trial
II. Evidence from one or more well-designed clinical trial without randomization; from cohort or case-controlled studies
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document titled "Anal Screening Evaluation."

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

For Kaposi's sarcoma and various types of lymphoma, including systemic non-Hodgkin's lymphoma (NHL), Hodgkin's disease, and primary central nervous system (CNS) lymphoma, the guidelines are based on the results of clinical trials, supplemented by the practical experience of experts in the field. For anal cancer and the non-acquired immunodeficiency syndrome (AIDS)-defining cancers, there are no therapeutic trials in human immunodeficiency virus (HIV)-infected adults to guide treatment; therefore, the guidelines are based on limited, primarily descriptive data in the literature.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and management of neoplastic complications in HIV-infected patients

POTENTIAL HARMS

Adverse Effects of Medications

- Myelosuppression is a potential overlapping toxicity when chemotherapy and highly active antiretroviral therapy (HAART) are co-administered. This is particularly true for HAART regimens that include zidovudine; therefore, it is generally recommended that zidovudine be avoided if at all possible during chemotherapy.
- Neuropathy is a common side effect of both vinca alkaloids and several antiretroviral (ARV) medications.
- High-dose methotrexate can cause significant mucositis, and transplant-conditioning regimens can cause both mucositis and protracted nausea and vomiting.
- Paclitaxel is associated with alopecia and neuropathy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with HIV infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers and consumers through mass mailings and numerous AIDS Institute-sponsored educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative, the AIDS Educational Training Centers (AETC) and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the New York State Department of Health (NYSDOH) Distribution Center for providers who lack internet access.

Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted through the Clinical Education Initiative (CEI) and the AIDS Education and Training Centers (AETC). The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-physician health

and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

IMPLEMENTATION TOOLS

Clinical Algorithm
Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Neoplastic complications of HIV infection. New York (NY): New York State Department of Health; 2007 Jul. 19 p. [39 references]

New York State Department of Health. Neoplastic complications of HIV infection. New York (NY): New York State Department of Health; 2007. 33 p. [94 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Jul

GUIDELINE DEVELOPER(S)

New York State Department of Health - State/Local Government Agency [U.S.]

SOURCE(S) OF FUNDING

New York State Department of Health

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site.

AVAILABILITY OF COMPANION DOCUMENTS

This guideline is available as a Personal Digital Assistant (PDA) download from the New York State Department of Health AIDS Institute Web site.

PATIENT RESOURCES

None available

NGC STATUS

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